REMARKS

Status of the Claims

Claims 1, 3-6, 8-11, 13-16, and 18-22 are pending in the present application. Claims 2, 7, 12, and 17 were previously canceled. Claims 10, 11, 13-16, and 18-22 are withdrawn as directed to a non-elected invention. Claim 21 is amended to correct an improper dependency. No new matter is added by way of this amendment. Reconsideration is respectfully requested.

Claim Objection

Claim 21 is objected to under 37 C.F.R. § 1.75(c), as depending on a canceled claim. Claim 21 is amended to depend on pending claim 1. Accordingly, the objection is overcome and Applicants respectfully request withdrawal.

Issues under 35 U.S.C. § 103(a)

Claims 1, 3-6, and 20

Basis for the rejection

Claims 1, 3-6, and 20 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Publication No. 2003/0060423 to Plata-Salaman, ("Plata-Salaman"), in view of U.S. Patent No. 5,643,905 to Moormann, ("Moormann"). Applicants respectfully traverse.

Specifically, the Examiner states that Plata-Salaman describes co-therapy compositions, *i.e.*, at least one compound of a general "formula I", which is administered with at least one acetylcholinesterase inhibitor, *e.g.*, galanthamine, *see* Office Action, page 6. In addition, the Examiner alleges that Plata-Salaman teaches that the compounds in the co-therapy composition are administered simultaneously, sequentially, separately, or in a single pharmaceutical formulation, *see* Office Action, page 6. The Examiner also asserts that Plata-Salaman teaches that, where dosing does not occur in a single formulation, the routes of administration may be varied to include, *e.g.*, intramuscular, transdermal, nasal, or parenteral administration. According to the Examiner, Plata-Salaman further teaches that unit dosage forms may be immediate release dosage forms, timed dosage forms, and sustained release dosage forms, *see* Office Action, page 6.

The Examiner admits that Plata-Salaman does not teach galanthamine or any of its salts as a sole medicament for either immediate or continuous release formulations, *see* Office Action,

page 6. In addition, the Examiner admits that Plata-Salaman does not describe using galanthamine to treat addictions. However, according to the Examiner, Moormann remedies these deficiencies. The Examiner states that Moormann describes using galanthamine and pharmaceutically acceptable salts thereof for treating addictive cravings, including nicotine dependence and alcohol withdrawal, *see* Office Action, page 7. The Examiner further states that Moormann expressly teaches continuous and controlled delivery methods of the drug including oral, transdermal, and parenteral modes, *e.g.*, intramuscular and nasal forms of administration, *see* Office Action, page 7.

The Examiner further admits that Moormann does not describe the combined administration of galanthamine, specified in the instant claims, *see* Office Action, page 7. However, according to the Examiner, upon review of the cited references, an ordinary artisan would have prepared such a formulation, *see* Office Action, page 7. The Examiner believes that an ordinary artisan would have been highly motivated to prepare the instantly claimed composition since galanthamine-based formulations may be separately co-administered as a continuous form and as an immediate oral or nasal solution form, as described by Plata-Salaman *see* Office Action, page 7. The Examiner also states that Moormann provides further motivation for the administration forms described in the present claims since this reference discloses a method for treating nicotine dependence with galanthamine *see* Office Action, page 7.

Standard for obviousness

When determining whether a claim is obvious, an examiner must make "a searching comparison of the claimed invention including all its limitations with the teaching of the prior art." *In re Ochiai*, 71 F.3d 1565, 1572 (Fed. Cir. 1995). Thus, "obviousness requires a suggestion of all limitations in a claim." *CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) (*citing In re Royka*, 490 F.2d 981, 985 (CCPA 1974)). Moreover, as the Supreme Court recently stated, "there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) (quoting In re Kahn, 441 F.3d 977, 988 (Fed. Cir. 2006)).

The present invention

Independent claim 1 is directed to a medicament for treating addiction craving, characterized in that the medicament consists of a combination of two administration forms, one of the administration forms continuously releasing at least one modulator of nicotinic receptors, which is selected from the group consisting of galanthamine and the pharmacologically acceptable salts of galanthamine, and the other administration form enabling a rapid entry of galanthamine or one of its pharmacologically acceptable salts into the central nervous system, wherein the administration form, which enables a quick entry of galanthamine, or a pharmacologically acceptable salt of galanthamine, into the central nervous system, is selected from the group consisting of: buccal solutions, spray solutions and drip solutions.

The cited art

Plata-Salaman teaches a co-therapy for the treatment of dementia and associated behavioral manifestations, such as memory disorders and behavioral, psychiatric, and/or psychological manifestations associated with dementia or a memory disorder, *see* abstract and paragraph [0020] of Plata-Salaman. Plata-Salaman's method comprises the administration of anticonvulsants and acetylcholinesterase inhibitors, such as galanthamine, *see* abstract and paragraph [0020]. As defined by Plata-Salaman "co-therapy", refers to treating a subject in need thereof by administering one or more compounds encompassed by the anticonvulsant of formula I and one or more acetylcholinesterase inhibitors, wherein said compounds and the acetylcholinesterase inhibitors are administered by any suitable means, *see* paragraph [0033] of Plata-Salaman.

Moormann teaches pharmaceutical formulations containing galanthamine or pharmaceutically acceptable salts thereof for treating nicotine dependence. Moormann further discloses that the described formulations allow for controlled release of the drug to the greatest possible extent, *see* column 2, lines 1 to 5.

The instant claims are not obvious in view of the cited references

As noted above, Plata-Salaman teaches a co-therapy for the treatment of dementia and associated behavioral manifestations, by administering anticonvulsants and acetylcholinesterase inhibitors. As previously described, "co-therapy", as defined by Plata-Salaman, means that one

or more anticonvulsant compounds of formula I, in combination with one or more acetylcholinesterase inhibitors, are administered by any suitable means, *see* paragraph [0033]. Based upon the foregoing, Plata-Salaman's definition clearly indicates that co-therapy refers to the administration of two different pharmaceutically active substances, selected from different groups of drugs, *i.e.*, an anticonvulsant and an inhibitor of acetylcholinesterase. Accordingly, in contrast to the instant claims, Plata-Salaman does not indicate that "co-therapy" means the simultaneous, sequential, or separate administration of the same pharmaceutically active substance by means of different administrative forms.

In further contrast to Plata-Salaman, the claimed compositions are for the treatment of addiction cravings, not for dementia and associated behavioral manifestations. Moreover, as the Examiner admits, Plata-Salaman does not teach the use of galanthamine or pharmacologically acceptable salts thereof as the sole pharmaceutically active substance to be administered in an immediate and/or continuous release formulation. In addition, Plata-Salaman fails to teach or suggest that addictions may be treated by administering galanthamine.

Moormann fails to remedy the deficiencies of Plata-Salaman. As noted above, Moormann describes pharmaceutical formulations for the treatment of nicotine dependence. Moorman discloses formulations, which allow for the controlled release of drugs to the greatest possible extent. However, the described formulations, *e.g.*, oral, transdermal, or other formulations, such as parenteral formulations, are intended for controlled release. Accordingly, Moormann does not teach or suggest any formulation of galanthamine or a pharmacologically acceptable salt thereof, which enables the rapid entry of an active ingredient into the central nervous system.

An ordinary artisan would have recognized from the Moormann disclosure that the treatments described therein are directed to basic cravings, not acute cravings. Applicants submit that acute cravings appear despite ongoing pharmaceutical withdrawal therapy. In this respect, Moormann only teaches one administration form of galanthamine or a pharmaceutically acceptable salt of galantamine, *i.e.*, a continuously releasing form. Accordingly, Moormann does not describe both of the administration forms described in the instant claims, *i.e.*, a continuous

and rapid release administration form. At least for this reason, Moormann is not able to remedy the deficiencies of Plata-Salaman and suggest the instant invention to an ordinary artisan.

Supplementing the teachings of Plata-Salaman with that of Moormann may have suggested to an ordinary artisan that acetylcholinesterase inhibitors, such as galanthamine, could have been administered by means of a formulation that would have allowed for the controlled release of the drug to the greatest possible extent. However, neither of these references, either alone or in combination, would have suggested to an ordinary artisan that the anticonvulsant described in Plata-Salaman should be omitted from the formulation. Moormann does not teach or suggest such omission. Further, Moormann does not teach or suggest substituting the anticonvulsant with galanthamine or a pharmacologically acceptable salt thereof. In addition, Moormann does not suggest that an additional dosage of galanthamine be further delivered *via* an administration form that allows for rapid entry of the drug into the central nervous system, as described in the present claims. Applicants submit that the Examiner has not articulated a reason which explains how Moormann suggests to an ordinary artisan that an additional galanthamine dosage should have been included in the formulation of Plato-Salamon.

As noted above, Plata-Salaman pertains to the treatment of dementia, memory disorders, behavioral, psychiatric, and/or psychological manifestations associated with dementia or a memory disorder. In contrast, Applicants wish to emphasize that the clamed invention is directed to the treatment of addiction cravings. For this reason alone, Plata-Salaman does not appear to be a suitable primary reference. Moormann does not remedy these deficiencies since an ordinary artisan could not have determined from Moormann that the co-therapy described in Plata-Salaman would have been useful for treating addictions. Nevertheless, even if it were, hypothetically, possible for an ordinary artisan to have interpreted Moorman as suggesting this use for Plato-Salaman's co-therapy, an ordinary artisan would not have been motivated by either reference to substitute the anticonvulsant described in the Plata-Salaman formulation with a second dose of galanthamine.

Moreover, Applicants submit that the present invention addresses a specific problem in the field of addiction treatment using pharmaceuticals, namely, the problem of acute cravings. This problem occurs despite any ongoing pharmaceutical treatment of addiction. The claimed

invention provides a means for addressing this problem. Although Moormann describes a method for treating nicotine dependence, the formulations described in Moormann are directed to a basic pharmaceutical therapy, *i.e.*, the formulations described in Moormann are for the controlled release of a drug. Accordingly, the formulations are not suitable for treating acute cravings, which as noted above, occur despite an ongoing pharmaceutical therapy.

Notably, Moormann does not address the problem of acute cravings that occur despite ongoing basal pharmaceutical withdrawal therapy. Further, Moormann does not teach or suggest combating acute cravings by employing an additional administration form, which allows for the rapid entry of galanthamine into the central nervous system.

At best, the Examiner's rejection amounts to little more than an improper class of "obvious to try" rejection. Specifically, the Examiner's rejection falls within the first of two classes of impermissible "obvious to try" rejections identified by the Federal Circuit.

In In re Kubin (2008-1184, decided April 3, 2009), the Federal Circuit recently revisited the issue of "obvious to try." The court highlighted an earlier decision of In re O'Farrell, 853 F.2d 894 (Fed. Cir. 1988), where it was cautioned that "obvious to try" is an incantation whose meaning is often misunderstood:

> It is true that this court and its predecessors have repeatedly emphasized that "obvious to try" is not the standard under § 103. However, the meaning of this maxim is sometimes lost. Any invention that would in fact have been obvious under § 103 would also have been, in a sense, obvious to try. The question is: when is an invention that was obvious to try nevertheless nonobvious?

In re O'Farrell, 853 F.2d 894, 903 (Fed. Cir. 1988).

The Federal Circuit held in In re Kubin that to differentiate between proper and improper applications of "obvious to try", it is necessary to understand two classes of situations where "obvious to try" is erroneously equated with obviousness under § 103. In the first class of cases,

> what would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.

Id. In such circumstances, where a defendant merely throws metaphorical darts at a board filled with combinatorial prior art possibilities, courts should not succumb to hindsight claims of obviousness. The inverse of this proposition is succinctly encapsulated by the Supreme Court's statement in KSR that where a skilled artisan merely pursues "known options" from a "finite number of identified, predictable solutions," obviousness under § 103 arises. 550 U.S. at 421.

The second class of O'Farrell's impermissible "obvious to try" situations occurs where what was "obvious to try" was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it. 853 F.2d at 903. Again, KSR affirmed the logical inverse of this statement by stating that § 103 bars patentability unless "the improvement is more than the predictable use of prior art elements according to their established functions." 550 U.S. at 417.

In the present instance, Applicants submit that the Examiner has participated in impermissible "obvious to try" analysis. Nowhere in the prior art is the particular requirements of the present claims actually suggested. While such a combination might hypothetically fall within the generic disclosure of the entirety of the cited art, the Examiner's rationale certain amounts to the throwing of metaphorical darts at a board filled with combinatorial prior art possibilities. This is the first of the two common "obvious to try" pitfalls decidedly admonished by the Federal Circuit.

Additionally, Applicants remind the Examiner that the fact that a claimed composition is within the broad field of the prior art and one might arrive at it by selecting specific items and conditions does not render the product obvious in the absence of some directions or reasons for making such selection. Ex parte Kuhn, 132 USPQ 359 (POBA 1961).

Based upon the foregoing, the instant claims are not obvious over the cited references. The cited references, either alone or in combination, at least, do not teach or suggest an administrative form for rapid release of galanthamine, or a pharmacological salt thereof, in combination with an administrative form for continuous release of galanathamine, or a pharmacological salt thereof, for the treatment of addiction cravings. Accordingly, withdrawal

of the rejection is respectfully requested.

Claims 5 and 6

Claims 5 and 6 are rejected under 35 U.S.C. § 103(a) as being obvious over Plata-Salaman with respect to claims 1, 3, and 4, *see* Office Action, pages 8-9. Applicants respectfully traverse.

As Applicant argued above, the combination of Plata-Salaman and Moormann, at least, does not teach or suggest an administrative form for rapid release of galanthamine, or a pharmacological salt thereof, in combination with an administrative form for continuous release of galanathamine, or a pharmacological salt thereof, as described in independent claim 1.

Dependent claims 5 and 6 incorporate all of the elements of independent claim 1. Accordingly, the instant claims are also not obvious over the cited references. Applicants respectfully request withdrawal of the rejection.

Claims 8 and 9

Claims 8 and 9 are rejected under 35 U.S.C. § 103(a) as allegedly obvious over U.S. Patent No. 2,906,265 to Samuels, ("Samuels"), with respect to claim 1, *see* Office Action, pages 9-10. Applicants respectfully traverse.

The Examiner states that claim 8 recites that the administration form for rapid entry is a flexible plastic container having a capacity between 1-5 ml. The Examiner further states that claim 9 limits claim 8, such that the plastic container is provided with nozzles through which the solution can be sprayed or dripped intra-nasally.

The Examiner admits that Plata-Salamon does not describe an actual device that contains and delivers the formulations described in the reference. However, the Examiner believes that an ordinary artisan would have used a flexible plastic container having a nozzle to intra-nasally deliver the instantly claimed galanthamine formulations. The Examiner makes this assertion because he believes that such containers are extremely well-known in the art. In support thereof, the Examiner cites Samuels, which describes nasal adaptor devices, having a nozzle and a base portion.

Claim 8 specifies that the administration form, which enables a rapid entry of galanthamine or a pharmacologically acceptable salt of galanthamine into the central nervous system, is in the form of a flexible plastic container with a capacity of between 1 and 5 ml.

As Applicants argued above, the combination of Plata-Salaman and Moormann, at least, do not teach or suggest an administrative form for rapid release of galanthamine, or a pharmacological salt thereof, in combination with an administrative form for continuous release of galanathamine, or a pharmacological salt thereof as described in independent claim 1. Dependent claims 8 and 9 incorporate all of the elements of independent claim 1. Samuels does not remedy the deficiencies of Plata-Salaman and Moormann. Samuels is merely cited for allegedly teaching the elements in the dependent claims 8 and 9. Accordingly, Applicants submit that the combination of cited references does not teach or suggest all of the elements of claims 8 and 9.

Notwithstanding the foregoing, Applicants further submit that Samuels teaches away from the use of the flexible plastic containers described in dependent claims 8 and 9. Samuels teaches pressurized, valved, dispensers, which may be made of flexible plastic, *see* column 2, lines 33-35 of Samuels. Conventional squeeze spray bottles are considered inefficient and unsatisfactory by Samuels, *see* column 1, lines 18-25 and 36-47. Accordingly, the teaching of Samuels would have caused a skilled artisan to refrain from using conventional squeeze spray bottles for releasing an administration form for solutions, which allows for a rapid entry of galanthamine or a pharmaceutically acceptable salt thereof. into the central nervous system.

Since pending claims 8 and 9 do not specify that the flexible plastic container is a pressurized, valved, container, but a flexible plastic container with nozzles, such that the solution therein can be dripped into the nose, Applicants submit that Samuels does not render the subject matter of pending claims 8 and 9 obvious to an ordinary artisan when considered in combination with Plata-Salaman and Moormann.

Based upon the foregoing, claims 8 and 9 are not obvious in view of the cited references. Withdrawal of the rejection is respectfully requested.

Request for Rejoinder

In view of the fact that the elected product claims are allowable, the Examiner is requested to rejoin the non-elected method claims, which include all limitations of the allowable products. Rejoinder is proper pursuant to MPEP § 821.04.

CONCLUSION

In view of the above, Applicants believe that the pending application is in condition for allowance.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact L. Parker, Reg. No. 46,046, at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37.C.F.R. §§1.16 or 1.17; particularly, extension of time fees.

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Respectfully submitted,

By _____

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